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Highly Enantioselective Intra- and Intermolecular [2 + 2] Photocycloaddition Reactions of 2-Quinolones Mediated by a Chiral Lactam Host: Host−Guest Interactions, Product Configuration, and the Origin of the Stereoselectivity in Solution

Thorsten Bach,*,† Hermann Bergmann,‡,|| Benjamin Grosch,† and Klaus Harms‡,⊥

Contribution from the Lehrstuhl für Organische Chemie I, Technische Universität München, D-85747 Garching, Germany and Fachbereich Chemie, Philipps-Universität Marburg, D-35032 Marburg, Germany

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Abstract: The [2 + 2] photocycloaddition of 4-alkoxy-2-quinolones was conducted in the presence of the chiral lactams **5** or *ent*-**5**. At −60 °C in toluene as the solvent the intramolecular reaction of quinolones **6** and **8** as well as the intermolecular photocycloaddition of various alkenes **13** to quinolone **12** proceeded with excellent enantioselectivity (81−98% ee) and in high yields (61−89%). Styrene (**13d**) reacted sluggishly in the intermolecular reaction (29% yield, 83% ee). The absolute configuration of the intramolecular photocycloaddition products **7** and **9** was elucidated by single-crystal X-ray crystallography of the corresponding diastereomeric *N*-menthyloxycarbonyl derivatives. The relative configuration of the intermolecular photocycloaddition products **14** and **15** was assigned on the basis of NOESY experiments and on crystallographic evidence. The differentiation of the enantiotopic faces in the prochiral quinolones **6**, **8**, and **12** can be explained by assuming a coordination of these substrates to the lactams **5** or *ent*-**5** via two hydrogen bonds. Upon binding to **5** the *si*-face is shielded by the bulky tetrahydronaphthalene backbone, and the *re*-face is exposed to an intra- or intermolecular attack. On the basis of the association constant (K_a) for the coordination of quinolone to host **5** an interpretation of the observed enantiomeric excess has been put forward. The parent quinolone **17** was employed as substrate for microcalorimetric and NMR titration experiments. From the data obtained for K_a and ΔH_a the expected enantiomeric excess was calculated for two given temperatures (−15 and −60 °C). The calculated values fit the observed data within reasonable limits and prove that two-point hydrogen bonding can be sufficient to achieve a preparatively useful face differentiation in solution phase photochemistry.

Introduction

Enantioselective reactions are defined as reactions in which prochiral substrates are converted to chiral enantiomerically pure or enantiomerically enriched products. In general, it is desirable to transfer the chiral information which eventually causes the enantioselectivity by a noncovalent interaction. Possible synthetic methods following this strategy are based on the stoichiometric use of chiral reagents or chiral complexing agents. The ultimate goal is to achieve highly enantioselective chemical transformations by substoichiometric amounts of chiral compounds, that is, by chiral catalysts. In particular, C−C-bond-forming reactions continue to attract the attention of organic chemists, and many enantioselective methods for the formation of C−C-bonds have emerged in recent years.[1] The development of enantioselective reactions in organic photochemistry lags behind the progress achieved in conventional organic chemistry. Whereas auxiliary-based stereoselective photochemical processes have been beautifully designed,[2] all attempts to induce enantioselective C−C-bond formation in solution either by chiral complexing agents,[3] by chiral reagents,[4] or catalytically, by chiral sensitizers[5] have seen limited success (<50% ee).[6,7]

* To whom correspondence should be addressed. E-mail: thorsten.bach@ch.tum.de.
† Technische Universität München.
‡ Philipps-Universität Marburg.
|| Current Address: Dr. Hermann Bergmann, Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK.
⊥ To whom inquiries about the X-ray analysis should be addressed at the University of Marburg.

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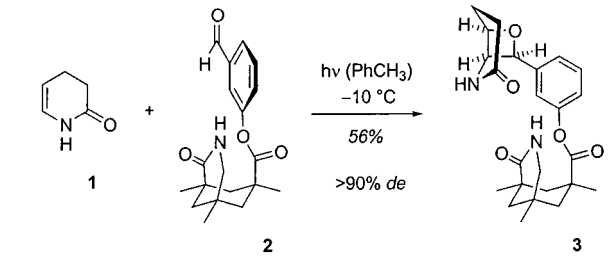
Photochemical reactions in the solid state have been more promising[8] and are a fascinating subject in their own right. Enantioselective intramolecular [2 + 2] photocycloaddition reactions,[9] intramolecular di-π-methane rearrangements,[10] pericyclic ring cyclization reactions,[11] and Norrish−Yang cyclizations[10a,12] represent a few significant reactions which were conducted in the solid phase with high enantioselectivity. The restricted movement of atoms and substituents in the solid state, however, severely hampers any general application of solid-state photochemistry. Rarely have enantioselective intermolecular photochemical reactions between two different reaction partners been reported in the solid state.[13]

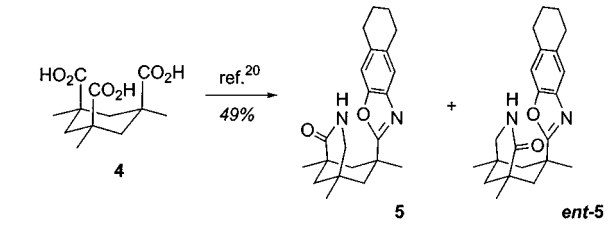
Our approach to achieve enantioselective reactions in solution is based on the use of chiral complexing agents (hosts). We planned to employ hydrogen bonds for the fixation of prochiral substrates to such a chiral host. In the environment of the host the photochemical reaction of the substrate was expected to occur in an enantioselective fashion. To facilitate the conversion of a broad array of substrates the binding site was constructed as simple and as general as possible. The key discovery was made in connection with our studies on the stereoselective Paternò−Büchi reaction of enamides (Scheme 1).[14] Dihydropyridone (**1**) underwent a photocycloaddition to the chiral aldehyde **2** to generate the oxetane **3** with perfect facial diastereoselectivity.[15]

It was unambiguously shown that the two hydrogen bonds which form between the lactam part of dihydropyridone **1** and the lactam unit of the aldehyde are responsible for the observed face discrimination. This discovery represented the first example

Scheme 1



Scheme 2



for facial stereocontrol in an intermolecular[16] photochemical reaction by hydrogen bonds,[17] and it has spurred increased interest in the use of hydrogen bonds as a control element in photochemical processes.[18] For us, the discovery proved that it should be possible to use systems related to **2** as chiral complexing agents. The benzoxazoles **5** and *ent*-**5** were consequently developed as readily accessible complexing agents. They offer a lactam binding site for coordination of an amide or a lactam substrate and a sterically demanding tetrahydronaphthalene backbone which shields one of the enantiotopic faces of a bound substrate. Their synthesis is easily accomplished in high yield starting from Kemp's triacid[19] (**4**) (Scheme 2).[20,21]

In the presence of **5** or *ent*-**5** highly enantioselective inter-[22] and intramolecular[23] [2 + 2] photocycloaddition reactions[24] have been conducted in solution.[25] The chiral information was almost completely transferred from the host to the corresponding

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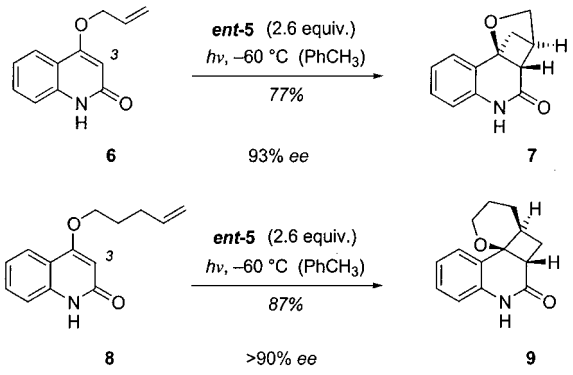
Scheme 3



substrates (82−98% ee). In the following account the key synthetic features of these reactions are provided in detail. The stereochemical outcome of the reaction is discussed, and data are presented which allow for a qualitative understanding of the host−substrate interaction.

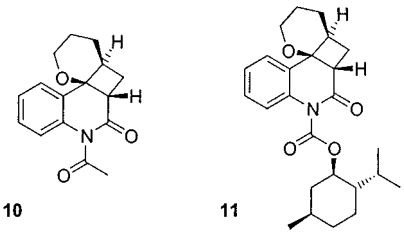
Results and Discussion

Photocycloaddition Results. The intramolecular [2 + 2] photocycloaddition of 4-alkenyloxy-2-quinolones has been studied intensively by Kaneko and co-workers.[26,27] We selected this reaction because it was reported to be a high-yielding process and the starting materials appeared to be well suited to bind to hosts **5** and *ent*-**5**. The regiochemistry of the photocycloaddition is unambiguous for quinolones with a 2-propenyloxy and a 4-pentenyloxy group in the 4-position. The former compound (**6**) yields exclusively the racemic crossed photocycloaddition product *rac*-**7**, and the latter compound (**8**) yields exclusively the racemic straight photocycloaddition product *rac*-**9** (cf. Scheme 3). Only a single diastereoisomer is formed. The preparation of the starting materials **6** and **8** has been reported and was achieved in five steps starting from quinoline.[27b,28]

When the photocycloaddition reaction was performed in the presence of the host compounds **5** or *ent*-**5**, significant enantioselectivities were recorded (Irradiaton source: Original Hanau TQ 150, immersion apparatus, Duran filter with 50% transmission at 320 nm, 10% transmission at 300 nm). The best results we achieved are summarized in Scheme 3. Relevant parameters for optimum selectivity include the use of a nonpolar solvent (toluene), a low irradiation temperature, and an excess of host. Experiments have been conducted varying the conditions. They give a rough picture as to the importance of the individual parameters. At room temperature, the enantioselectivity achieved in the reaction **6** → **7** was 39% ee if toluene was employed as the solvent (2.1 equiv of host). In acetonitrile, the enantioselectivity dropped significantly (4% ee) under otherwise indentical conditions. At −15 °C the observed enantioselectivity was 84% ee if 2.6 equiv of the host was employed in toluene as the solvent. If only 1 equiv of the host was used under otherwise identical conditions the decrease in enantioselectivity was detectable but moderate (78% ee). Although the solvent influence is certainly the most dramatic, we could not, due to the limited solubility of the host, further decrease the solvent polarity, for example, by using pentane or hexane. Quantitative considerations concerning the temperature and the host concentration will be discussed in a later section.

In the case of photocycloaddition product **7** the enantiomeric excess could be determined by chiral HPLC (Chiracel OD; eluent: hexane/*i*-propanol = 92/8). The enantiomeric excess of compound **9** could not be directly assessed. It was eventually quantified by ^{1}H NMR spectroscopy. To this end, the quinolone was *N*-acylated (Ac_2O in pyridine) to yield imide **10**, the enantiomeric excess of which could be determined by shift experiments. Tris-(3-heptafluoropropylhydroxymethylene-(+)-camphorato)europium [Eu(hfc)$_3$] proved to be the reagent of choice. The detection limit for compound *ent*-**10** in the presence of a large excess of its enantiomer **10** proved to be higher than it was in the HPLC experiments. We consequently report a value of >90% ee if the other enantiomer was not detectable by ^{1}H NMR spectrocscopy.

The absolute configuration of the products was unambiguously proven by single crystal X-ray crystallography. The enantiomerically pure compound **9** was converted to its *N*-menthyloxycarbonyl derivative **11** by successive treatment with *n*-BuLi and (−)-menthylchloroformate in THF. The absolute configuration was deduced from the known configuration of the menthyl residue. The structure of compound **11** in the crystal is depicted in Figure 1. In a fully analogous fashion, the absolute configuration of compound **7** was deduced from its *N*-menthyloxycarbonyl derivative.[29]



The assigned absolute configurations are in line with a complexation of substrates **6** and **8** to the host *ent*-**5** via hydrogen bonds as shown in Scheme 5 (vide infra). An intramolecular attack at the quinolone double bond can occur exclusively from the *si*-face relative to carbon atom C-3. The other face is shielded by the bulky tetrahydronaphthalene unit. In this context, it should be mentioned that we initially intended to use a naphthalene unit as a fully planar and possibly more effective shield. The corresponding host is equally well accessible[20] but exhibits a long wavelength absorption at 290 nm (ϵ = 7200), 301 nm (ϵ = 8700), and at 327 nm (ϵ = 2000). In attempted photocycloaddition reactions of substrate **6** there was no product formation at λ = 300 nm (Rayonet RPR 3000 Å) after 1 h at room temperature (solvent: toluene). Apparently, the host prevents the photocycloaddition acting as a more efficient absorber than the quinolone **6**. Photosensitization was not observed. As an additional consequence, the host was partially destroyed (75% recovery yield). In strong contrast, the hosts **5** and *ent*-**5** exhibit no long wavelength ($\lambda \geq$ 300 nm) absorption and are fully recovered after the photocycloaddition (>95% recovery yield).

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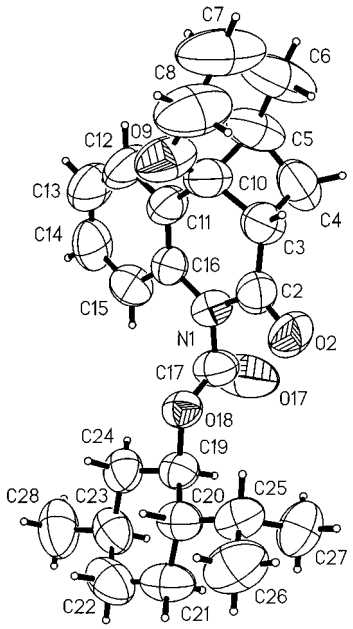
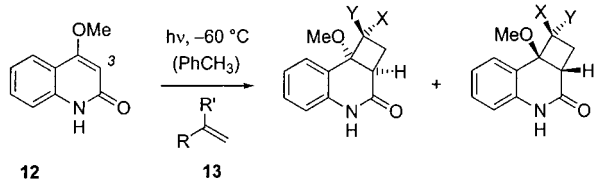


Figure 1. Structure of compound **11** in the crystal.

Scheme 4



13a	R = $CH_2CH_2CH_2OH$	R' = H	**14**	X = R, Y = H	*ent*-**14**
13b	R = CH_2OAc	R' = H			
13c	R = OAc	R' = H	**15**	X = H, Y = R	*ent*-**15**
13d	R = Ph	R' = H			
13e	R = COOMe	R' = H			
13f	R = CH_2CH_3	R' = CH_2CH_3	**14f**		*ent*-**14f**

A major benefit of the use of chiral complexing agents in solution is associated with the fact that they can be equally employed for intermolecular reactions. To demonstrate this ability we studied the [2 + 2] photocycloaddition of 4-methoxy-2-quinolone (**12**) and various alkenes **13**. Again, previous work by Kaneko et al. had established that these substrates react with high chemo- and regioselectivity to yield the corresponding cyclobutanes in racemic form.[27,30] In Scheme 4 the reactions we have conducted are summarized. Table 1 provides the results under optimized irradiation conditions. The truly remarkable aspect is the high enantioselectivity achieved in all instances. Every major product is formed in an enantiomeric excess >81% ee. These enantioselectivities are unprecedented for an intermolecular photochemical reaction. The enantiomeric excess was determined by chiral HPLC (Chiracel OD; eluent: hexane/*i*-propanol = 92/8). Compound **14e** and *ent*-**14e** had to be reduced to the corresponding alcohol ($LiBH_4$ in THF/EtOH) before a satisfactory HPLC separation was achieved (entry 6). Replacing host **5** by its enantiomer *ent*-**5** resulted in a reversal of the product enantioselectivity (entries 2 and 3). In the case of the terminal alkenes **13a**−**13e** two diastereoisomers **14** and **15** (and their enantiomers *ent*-**14** and *ent*-**15**) can be formed. The simple diastereoselectivity in favor of the *exo*-isomers **14** and *ent*-**14** was high for alkenes **13a**, **13b**, and **13e** (entries 1−3, 6). Styrene favored the formation of the *endo*-diastereoisomers **15** and *ent*-**15** (entry 5), whereas the use of vinyl acetate (**13c**) resulted in a mixture of diastereoisomers (entry 4). The 1,1-disubstituted alkene **13f**, of course, gave only a single product (entry 7). It was shown in control experiments that the simple diastereoselectivity is not significantly altered by the host.

Table 1. Enantioselective Intermolecular [2 + 2] Photocycloaddition of the 2-Quinolone **12** in the Presence of the Chiral Host Compounds **5** and *ent*-**5**

entry	substrate	host	dr[a] (**14**/**15**)	yield [%][b]	product	ee [%][c]
1	**13a**	**5**	> 95/5	80	**14a**	81
2	**13b**	**5**	> 95/5	80	**14b**	92
3	**13b**	*ent*-**5**	> 95/5	81	*ent*-**14b**	91
4	**13c**	*ent*-**5**	63/27	89	*ent*-**14c**	93
					ent-**15c**	98
5	**13d**	**5**	< 5/95	29[d]	**15d**	83
6	**13e**	**5**	90/10	84	**14e**	82
7	**13f**	**5**	−	61	**14f**	92

[a] The diastereomeric ratio of cyclobutanes in the crude product was determined by integration of appropriate ^{1}H NMR signals. [b] Yield of isolated product. [c] The enantiomeric excess was determined by chiral HPLC (Chiracel OD; eluent: hexane/*i*-propanol = 92/8). [d] The reaction remained incomplete even upon prolongued irradiation; 65% of the quinolone was recovered.

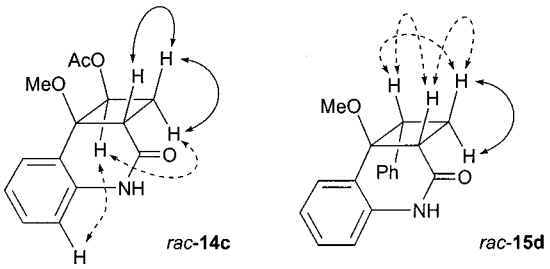


Figure 2. Strong (—) and medium (- - -) ^{1}H NOESY contacts recorded for compounds *rac*-**14c** and *rac*-**15d**.

The assignment of the absolute configuration was based on our previous results obtained in the intramolecular reaction of 2-quinolones (vide supra). The use of host **5** accordingly induces a *re*-attack at carbon atom C-3, and the host *ent*-**5** induces a *si*-attack. The optical rotation of the products was in full agreement with the tentative assignment. Compound **14a** which was obtained from the photocycloaddition in the presence of host **5** was dextrorotary, whereas the structurally related intramolecular photocycloaddition product **9** which was formed in the presence of host *ent*-**5** was levorotatory. Although the relative configuration had been assigned previously for *rac*-**14** and *rac*-**15** on the basis of coupling constants,[30a] we examined all major diastereoisomers by ^{1}H NOESY experiments. The significant NOESY contacts of the major diastereoisomers *rac*-**14c** and *rac*-**15d** are depicted in Figure 2. Additional proof for the assignment of compound *rac*-**14a** was obtained by single-crystal X-ray crystallography. After silylation (TBDMSCl, imidazole in CH_2Cl_2) the corresponding silyl ether *rac*-**16** delivered suitable crystals (Figure 3). Unfortunately, only the racemic product was crystalline, a fact which precluded the determination of the absolute configuration.

Titration Experiments. An insight into the mechanism of action of hosts **5** and *ent*-**5** was expected by looking more closely at their complexation to 2-quinolones. The low solubility of

(30) (a) Kaneko, C.; Naito, T. *Chem. Pharm. Bull.* **1979**, *27*, 2254. (b) Naito, T.; Kaneko, C. *Chem. Pharm. Bull.* **1983**, *31*, 366. (c) Sato, M.; Kawakami, K.; Kaneko, C. *Chem. Pharm. Bull.* **1987**, *35*, 1319.

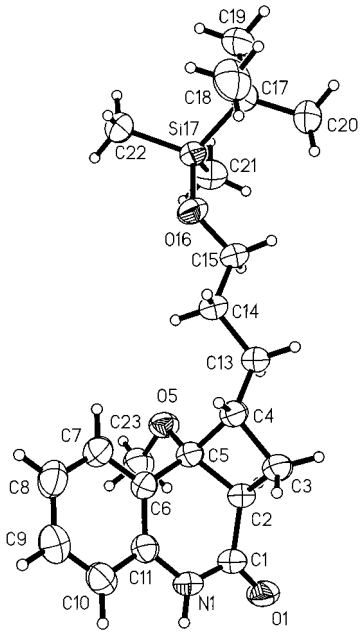
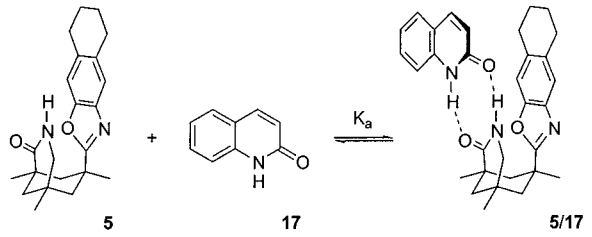


Figure 3. Structure of compound *rac*-**16** in the crystal.

Scheme 5



4-alkoxy-2-quinolones in toluene made us use the parent compound, 2-quinolone (**17**), as a model system to study a potential host−substrate complex. Since the bulky tetrahydronaphthalene units would severly interact upon self-association (dimerization) of enantiomerically pure host **5**, its dimerization constant is close to zero. This was confirmed by NMR titration experiments conducted in toluene at 20 °C. Upon titration of quinolone **17** with host **5** under the same conditions a strong and pronounced shift change of the NH protons in both compounds **17** and **5** was observed. A Job plot of the product of shift change $\Delta\delta_{NH}$ (**5**) and mole fraction X of compound **5** defined as $c_0(\mathbf{5})/[c_0(\mathbf{5}) + c_0(\mathbf{17})]$ against the mole fraction X showed a maximum at 0.5, indicating a 1:1 binding. Our interpretation of this result is a complexation of quinolone **17** to compound **5** as indicated in Scheme 5 via two hydrogen bonds (see also Figure 4).

The determination of the association constant K_a for the formation of complex **5**/**17** from the binding isotherm of the titration was complicated by the fact that the dimerization constant of compound **17** remained unknown. The low solubility in toluene prevented a direct determination. The dimerization constant was assessed by optimizing the curve fit of the binding isotherm **5**/**17** as $K_{dim} = 41\ M^{-1}$. For all quantitative interpretations of the titration data the HOSTEST program[31] was used. The order of magnitude for the dimerization constant is in line with an earlier value which we obtained for the self-association

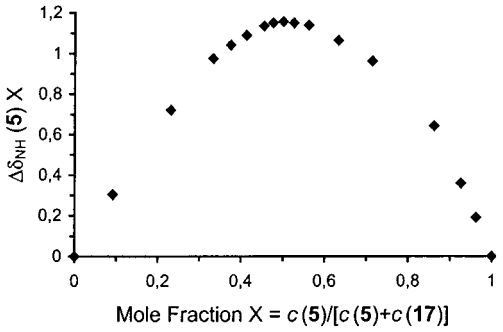


Figure 4. Job plot analysis of δ_{NH} (**5**) in toluene at 20 °C for the system **5**/**17**.

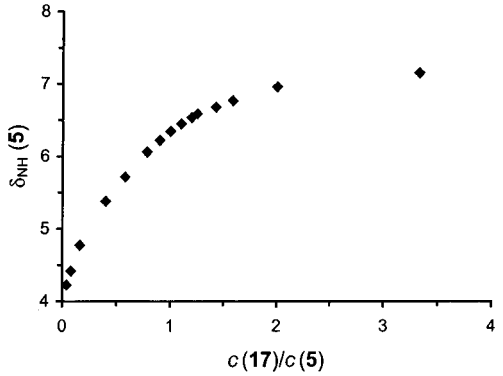


Figure 5. NMR-titration of compound **5** and quinolone **17** at 20 °C in toluene as the solvent.

of dihydropyridone. This more soluble unsaturated six-membered lactam displayed a dimerization contant of $K_{dim} = 85\ M^{-1}$ at −10 °C in toluene as the solvent.[15] Other values found in the literature for the dimerization of quinolones[32] have been determined in chloroform solution and are therefore difficult to compare. From the binding isotherm depicted in Figure 5 we calculated the bimolecular association constant K_a for **5**/**17** (Scheme 5) as 580 M^{-1}.

We attempted to gain further information on the association of **5** and **17** from microcalorimetry measurements. These titrations were conducted by adding a concentrated solution of host **5** in toluene (220 mM) to a dilute solution (10 mM) of substrate **17** in toluene. The data were recorded at 30 °C. The self-association of compound **17** is small under the chosen conditions.[33] The heat pulse results from the association of compounds **5** and **17**. The association enthalpy ΔH_a is determined as the integral of the individual heat pulses. The process of breaking potential dimers of compound **17** is endothermic and should—if it plays any role at all—lead to a value for ΔH_a which is higher (less negative) than the real value. In this respect, the determined value $\Delta H_a = -11.8$ kJ mol^{-1} represents an upper barrier. All thermodynamic data were processed by an integration and curve fit program implemented in the calorimeter (see Experimental Section). The free association enthalpy was also assessed by this means and is roughly in line with the value obtained from the titration data.[34]

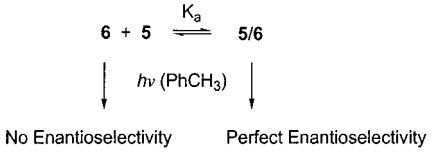
As already alluded to above, the data obtained from NMR and microcalorimetric titration experiments are only estimates,

(31) Wilcox, C. S. In *Frontiers in Supramolecular Chemistry and Photochemistry*; Schneider, H.-J., Dürr, H., Eds.; VCH: Weinheim, 1991; p 123.

(32) Zimmermann, S. C.; Duerr, B. F. *J. Org. Chem.* **1992**, *57*, 2217 (K_{dim} = 46 M^{-1} for a 3,4-dialkyl substituted quinolone in $CHCl_3$).

(33) Assuming $K_{dim} = 41\ M^{-1}$ the concentration of monomeric **17** would be ca. 6.6×10^{-3} M and the concentration of dimeric $(\mathbf{17})_2$ would be 1.7×10^{-3} M.

Scheme 6



$$(1)\quad ee = \frac{c(\mathbf{5/6}) + c(\mathbf{6})/2 - c(\mathbf{6})/2}{c(\mathbf{5/6}) + c(\mathbf{6})} = \frac{c(\mathbf{5/6})}{c_0(\mathbf{6})}$$

$$(2)\quad ee = \frac{K_a\, c(\mathbf{5})}{1 + K_a\, c(\mathbf{5})}$$

but taken together, they yield some important information. First, the association constant K_a for the formation of complex **5**/**17** as depicted in Scheme 5 is in the order of 500 M^{-1} at 293 K. Even if one concedes a high error margin to this value, it is about 1 order of magnitude higher than the dimerization constant of compound **17** $K_{dim} \cong 50\ M^{-1}$. Second, the association enthalpy ΔH_a for the formation of **5**/**17** can be estimated at an upper limit of $\Delta H_a \leq -11.8$ kJ mol^{-1}.

Temperature Dependence. A simple model can be devised to account for the observed enantioselectivities in the [2 + 2] photocycloaddition reactions. It was assumed that there is a 1:1 binding of a 4-alkoxy-2-quinolone such as **6** and host **5** and that the enantioselectivity is perfect upon complexation and zero if the quinolone was not coordinated (Scheme 6). As the irradiation experiments were conducted with an initial substrate concentration $c_0(\mathbf{6}) = 5 \times 10^{-3}$ M, the dimerization of compound **6** was not implemented. The enantioselectivity expressed as ee depends on the relative concentration of the complex **5**/**6** and of the free quinolone **6** [eq 1]. Alternatively, the ee can be expressed as a function of the association constant K_a and of the host concentration c(**5**) [eq 2]. In this equation the decisive parameters and their influence on the ee are obvious. If K_a and c(**5**) is high, the ee value will be high. A nonpolar solvent and a low reaction temperature lead to an increased association which in turn increases the enantioselectivity. As the initial concentration of host c_0(**5**) correlates with c(**5**), the importance of the host concentration c_0(**5**) can be analogously explained.

By applying van't Hoff's equation the association constants K_a were calculated for different temperatures. From these values and from the initial concentrations of **5** and **6**, c_0(**5**) and c_0(**6**), a calculation of the expected ee at a certain temperature is possible.[35] This calculated ee corresponds to the ratio of the concentration of complex **5**/**6** relative to the total concentration of compound **6** in solution. If this was done for the photochemical reactions **6** → **7** discussed earlier, a decent correlation was obtained. At −60 °C under the conditions given in Scheme 3 [$c_0(\mathbf{5}) = 1.3 \times 10^{-2}$ M and $c_0(\mathbf{6}) = 5 \times 10^{-3}$ M] the calculated ee is for example $ee_{calc} = 97\%$ ($ee_{obs} = 93\%$). At −15 °C employing identical concentrations (vide supra) the calculated ee is $ee_{calc} = 90\%$ ($ee_{obs} = 84\%$). In general, the calculated values are higher than the values indeed recorded, indicating either that the enantioface differentiation is not perfect or that the dimerization of quinolones cannot be fully neglected even at concentrations of 5×10^{-3} M.

(34) The microcalorimetry data suggest a 2:1 binding of **5** to **17**. This is contrary to the results of the NMR titration which clearly indicate that there is 1:1 binding due to hydrogen bonds. As any other binding phenomenon but hydrogen bonding is not detected by NMR, it is not unlikely that there is an additional interaction between a second host molecule **5** and the complex **5**/**17**. The average free association enthalpy for the two binding processes was determined by microcalorimetry as $\Delta G_a = -13.5$ kJ mol^{-1} at 303 K.

(35) Strictly, eqs 1 and 2 are only valid at the beginning of the reaction. Provided that product **7** exhibits an association similar to substrate **6**, the equations remain valid throughout the reaction.

Conclusions and Outlook

In summary, highly enantioselective intra- and intermolecular [2 + 2] photocycloaddition reactions of 4-alkoxy-2-quinolones were conducted in the presence of a designed chiral lactam host. The carbonyl group of the lactam acts as hydrogen acceptor, and the NH group acts as hydrogen donor. Key to the success of these reactions is the fact that the host binds the substrates effectively via two hydrogen bonds. By this means, the substrates are held in a chiral environment which in turn enables the enantioface differentiation. For an effective host−substrate recognition it is further important that the substrate binds more strongly to the host than to itself (self-association). For the system under scrutiny, the thermodynamic data (K_a, ΔH_a) obtained by NMR titration and microcalorimetry are in line with a high enantiomeric excess (up to 97% ee). It was demonstrated that the calculated ee values fit the experimental values reasonably well.

Further studies to extend the application of the hosts for photoinduced processes are under way in our laboratories. In this respect, new photochemical reactions of lactams and amides are being investigated. Improved ligands are being constructed whose binding is even more efficient. Catalytic applications are being studied. Results of this endeavor will be reported in due course.

Experimental Section

General Information. All reactions involving water-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under Ar. Irradiation experiments were performed in Merck p.a. solvents. Pyridine was distilled from calcium hydride. Common solvents [*tert*-butyl methyl ether (TBME), pentane (P), methanol, ethanol, CH_2Cl_2] were distilled prior to use. All other reagents and solvents were used as received. TLC was performed on aluminum sheets (0.2 mm silica gel 60 F_{254}) with detection by UV (254 nm) or by coloration with ceric ammonium molybdate (CAM). Flash chromatography was performed on silica gel 60 (Merck, 230−400 mesh) (ca. 50 g for 1 g of material to be sparated) with the indicated eluent. HPLC analyses were performed with chiral columns (Chiracel OD; Daicel Chemical Industries) employing *n*-hexane/2-propanol as eluents (flow rate: 1.0 mL/min) and UV-detection. IR: Nicolet 510M FT-IR or Perkin-Elmer 1600 FT-IR. MS: Varian CH7 (EI). HRMS: Finnigan MAT 95S or MAT 8200. GC−MS: Agilent 6890 (GC system), Agilent 5973 (mass-selective detector). Elementary analysis: Varian Elementar vario EL. ^{1}H and ^{13}C NMR: Bruker ARX-200, AC-250, AC-300, AMX-400, and AMX-500. ^{1}H and ^{13}C NMR spectra were recorded at 303 K unless stated otherwise. Chemical shifts are reported relative to tetramethylsilane as an internal reference. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of magnetically nonequivalent protons are marked as virtual (virt.). The multiplicities of the ^{13}C NMR signal were determined by DEPT experiments. NOESY contacts are reported as weak (′), medium (″), or strong (‴).

Preparation of Starting Materials. The chiral host compounds **5** and *ent*-**5** were prepared as previously described[20] and employed in

enantiomerically pure form (>95% ee). The quinolones **6**,[27b] **8**,[27b] and **12**[36] were synthesized according to reported procedures.

General Irradiation Procedure for the Intramolecular [2 + 2] Photocycloaddition. A solution of the 2-quinolone **6** or **8** ($c = 5 \times 10^{-3}$ M) and of the chiral host **5** or *ent*-**5** in toluene was irradiated in Duran tubes (light source for the reactions at 30 °C: Rayonet RPR 3000, $\lambda = 300$ nm; light source for the reactions at −15 and −60 °C: Original Hanau TQ 150, Duran filter). After complete conversion (1−4 h) the solvent was removed in vacuo, and the residue was purified by flash chromatography (TBME/P = 1/2 → 2/1). The enantiomeric excess was determined by chiral HPLC (**7**, *n*-hexane/*i*-propanol = 92/8) or after derivatization (**9**) by ^{1}H NMR-shift experiments.

3,3a,4,5-Tetrahydro-3,9b-methanofuro[3,2-*c*]quinolin-4(2*H*)-one (7 and *ent*-7):[27b] previously unreported analytical data: mp 177−179 °C; $R_f = 0.50$ (EtOAc); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 40.7$ (t, Ar*C*CH_2), 42.3 (d, NHCOCH*C*H), 52.6 (d, NHCO*C*H), 71.9 (t, OCH_2), 86.7 (s, Ar*C*), 115.5 (d, CH_{ar}), 121.7 (s, C_{ar}), 123.7 (d, CH_{ar}), 123.8 (d, CH_{ar}), 129.0 (d, CH_{ar}), 136.9 (s, C_{ar}), 171.1 (s, CO).

(−)-*ent*-**7**: HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 20.6$ min; $[\alpha]^{20}_D = -20.3$ (*c* 1.5, CH_2Cl_2) [39% ee]. (+)-**7**: HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 23.8$ min.

Benz[*k*]-10-aza-2-oxatricyclo[6.4.0.0^{1,6}]undecan-9-one (9 and *ent*-9):[27b] previously unreported analytical data: mp 203−205 °C; $R_f = 0.38$ (EtOAc); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 23.3$ (t, OCH_2CH_2), 25.5 (t, $NHCOCHCH_2$), 27.5 (t, $OCH_2CH_2CH_2$), 40.2 (d, NHCO*C*H), 40.6 (d, $NHCOCHCH_2CH$), 63.2 (t, OCH_2), 72.3 (s, Ar*C*), 115.9 (d, CH_{ar}), 123.8 (d, CH_{ar}), 126.3 (s, C_{ar}), 128.8 (d, CH_{ar}), 129.2 (d, CH_{ar}), 136.2 (s, C_{ar}), 170.8 (s, CO).

(−)-*ent*-**9**: HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 26.5$ min; $[\alpha]^{20}_D = -13.2$ (*c* 1.06, CH_2Cl_2) [16% ee]. (+)-**9**: HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 26.5$ min; $[\alpha]^{20}_D = +68.2$ (*c* 0.58, CH_2Cl_2) [>90% ee].

***N*-Acetyl Lactam 10 by Acetylation of Compounds 9 and *ent*-9.** A solution of lactam **9** (50 mg, 0.22 mmol) in pyridine (2 mL) and acetic acid anhydride (1 mL) was heated under reflux for 2.5 h. The solution was allowed to cool to room temperature and partitioned between CH_2Cl_2 (10 mL) and water (10 mL). The layers were separated, and the organic layer was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were washed with 2 M HCl (2 × 10 mL), saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL) and dried over $MgSO_4$. After filtration the solvents were removed in vacuo. Purification of the crude product by flash chromatography (TBME/pentane = 2/1) gave a colorless oil (30 mg, 50%). $R_f = 0.33$ (TBME/pentane = 1/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.66−1.75 (m, 3 H, C*HH*, C*H*H), 1.78−1.85 (m, 1 H, C*H*H) 1.88−1.96 (m, 1 H, CH*H*), 2.22−2.29 (m, 1 H, CH*H*), 2.46−2.52 [m, 1H, C*H*$(CH_2)_2$], 2.59 (s, 3H, CH_3), 3.81−3.87 (m, 1H, OC*H*H), 3.90 (virt. t, $^3J = 9.6$ Hz, 1H, NCOC*H*), 3.94−4.00 (m, 1H, OCH*H*), 7.12 (dd, $^3J = 8.3$ Hz, $^4J = 0.9$ Hz, 1H, arom. H), 7.20−7.32 (m, 2H, arom. H), 7.52 (dd, $^3J = 7.7$ Hz, $^4J = 1.5$ Hz, 1H, arom. H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.1 (t, CH_2), 25.2 (t, CH_2), 27.0 (t, CH_2), 28.1 (q, CH_3), 40.3 (d, CH), 41.8 (d, CH), 63.5 (t, OCH_2), 72.0 (s, *C*OCH_2), 118.5 (d, CH_{ar}), 125.2 (d, CH_{ar}), 128.6 (s, C_{ar}), 128.8 (d, CH_{ar}), 129.0 (d, CH_{ar}), 135.0 (s, C_{ar}), 170.3, 176.0 (s, 2C, CONCO); HRMS (EI) calcd for $C_{16}H_{17}NO_3$ 271.1208, found 271.1206; for C_{15}-$^{13}C_1H_{17}NO_3$ calcd. 272.1242, found 272.1244.

***N*-Menthyloxycarbonyllactam 11 by Acylation of the Enantiomerically Pure Compound 9.** To a solution of amide (+)-**9** (76 mg, 0.33 mmol) [>90% ee] in THF (15 mL) at −78 °C was added dropwise *n*-BuLi (0.24 mL, 1.55 M in *n*-hexane, 0.36 mol). After 30 min, (−)-menthyl chloroformate (84 μL, 87 mg, 0.40 mmol) was added. The mixture was maintained at −78 °C for 45 min and then for another hour at 0 °C. The reaction was quenched by the addition of saturated aqueous NH_4Cl (1 mL), and the solvent was removed in vacuo. The residue was partitioned between CH_2Cl_2 (20 mL) and saturated aqueous $NaHCO_3$ (5 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL) and dried over $MgSO_4$. After filtration the solvents were removed in vacuo. Purification of the crude product by flash chromatography (TBME/pentane = 1/7) gave a white solid (54 mg, 40%, >90% de). $R_f = 0.36$ (TBME/pentane = 1/1); HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 10.4$ min; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (d, $^3J = 6.8$ Hz, 3H, CH_3-menthyl), 0.90−0.96 (m, 1H), 0.91 (d, $^3J = 6.9$ Hz, 3H, CH_3-menthyl), 0.97 (d, $^3J = 6.5$ Hz, 3H, CH_3-menthyl), 1.05−1.21 (m, 2H), 1.40−1.50 (m, 1H), 1.50−1.60 (m, 1H), 1.60−1.80 (m, 2H), 1.80−1.90 (m, 2H), 2.07−2.17 (m, 1H), 2.23−2.33 (m, 2H), 2.41−2.51 (m, 1H), 3.82 (virt. t, $^3J = 9.7$ Hz, 1H, OC*H*H), 3.92−4.05 (m, 2H), 4.90 (virt. dt, $^3J = 10.9$ Hz, $^3J = 4.2$ Hz, 1H, COOCH), 6.78 (d, $^3J = 8.2$ Hz, 1H, arom. H), 7.19 (virt. t, $^3J = 7.4$ Hz, 1H, arom. H), 7.30 (virt. t, $^3J = 7.5$ Hz, 1H, arom. H), 7.50 (d, $^3J = 7.7$ Hz, 1H, arom. H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.8 (q, CH_3-menthyl), 20.7 (q, CH_3-menthyl), 21.9 (q, CH_3-Menthyl), 22.9 (t, CH_2), 23.2 (t, CH_2), 25.2 (t, CH_2), 25.6 (d, CH), 27.3 (t,CH_2), 31.5 (d, CH), 34.0 (t, CH_2), 39.8 (t, CH_2), 40.3 (d, CH), 40.8 (d, CH), 46.6 (d, CH), 63.2 (t, OCH_2), 71.9 (q, $COCH_2$), 80.0 (d, COO*C*H), 114.9 (d, CH_{ar}), 124.4 (d, CH_{ar}), 126.8 (s, C_{ar}), 129.2 (d, CH_{ar}), 129.4 (d, CH_{ar}), 135.2 (s, C_{ar}), 153.1, 167.0 (s, 2C, NCOO, NCO); Anal. Calcd for $C_{25}H_{33}NO_4$: C, 72.96; H, 8.08; N, 3.40. Found: C, 72.51; H, 7.83; N, 3.39.

Single-crystal X-ray crystallography of compound 11: crystal data of compound **11** ($C_{25}H_{33}NO_4$, $M_r = 411.52$): crystal size 0.50 × 0.45 × 0.30 mm^3, tetragonal, space group $P4_12_12_1$, $a = b = 941.6(2)$ pm, $c = 5133.1(14)$ pm, $\alpha = \beta = \gamma = 90$ °, $U = 4551(4)$ Å^3, $D_c = 1.201$ g cm^{-3} for $Z = 2$, $F(000) = 1776$, $\mu = 0.643$ mm^{-1}, Enraf Nonius CAD4 diffractometer, $\lambda = 1.54178$ Å, $T = 213$ K, ω-scan, 4261 reflections ($-h$, $+k$, $\pm l$), $\Theta_{max} = 60.0°$, 3389 independent and 2381 observed reflections [$F \geq 4\sigma(F)$], 275 refined parameters, R = 0.0628 (observed data), w$R^2 = 0.1863$ (independent data), residual electron density 0.190 eÅ^{-3}, direct methods, hydrogen atoms calculated (SHELXS-97, SHELXL-97, SHELXTL). Crystallographic data for the structures reported in this work have been deposited as a CIF file (see Supporting Information).

General Irradiation Procedure for the Intermolecular [2 + 2] Photocycloaddition. A solution of 4-methoxy-2-quinolone (**12**) ($c = 5 \times 10^{-3}$ M), 20 equiv of the alkene (50 equiv in the case of styrene) and of the chiral host **5** or *ent*-**5** in toluene was irradiated (light source for the reactions at 30 °C: Rayonet RPR 3000, $\lambda = 300$ nm; light source for the reactions at −20 and −60 °C: Original Hanau TQ 150, Duran filter). After complete conversion the solvent and the excess alkene was removed in vacuo, and the residue was purified by flash chromatography. A complete separation of the chiral host and the products **14c**/**15c**, **15d**, and **14f** was not possible. In these cases the ratio of product and residual host in the mixture was determined by integration of appropriate ^{1}H NMR signals. The diastereomeric ratio, dr (**14**/**15**), was determined by integration of appropriate ^{1}H NMR signals in the crude product mixture. The enantiomeric excess was determined by chiral HPLC (*n*-hexane/*i*-propanol = 92/8).

1-(3′-Hydroxypropyl)-8b-methoxy-2,2a,4,8b-tetrahydro-1H-cyclobuta[*c*]quinolin-3-one (14a and *ent*-14a):[27b] previously unreported analytical data: $R_f = 0.27$ (EtOAc); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.9 (t, $HOCH_2CH_2CH_2$), 26.1 (t, $NHCOCHCH_2$), 30.8 (t, $HOCH_2CH_2$), 41.6 (d, NHCO*C*H), 47.1 (d, $NHCOCHCH_2CH$), 50.4 (q, CH_3), 62.8 (t, $HOCH_2$), 77.2 (s, *C*OMe), 115.6 (d, CH_{ar}), 124.1 (d, CH_{ar}), 124.5 (s, C_{ar}), 128.0 (d, CH_{ar}), 129.4 (d, CH_{ar}), 137.3 (s, C_{ar}), 171.6 (s, CO); MS (EI), *m*/*z* (%) 175 (100), 149 (2), 132 (5), 117 (5), 55 (3).

(−)-**14a**: $[\alpha]^{20}_D = -24.9$ (*c* 1.0, CH_2Cl_2) [74% ee]; HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 31.3$ min. (+)-*ent*-**14a**: HPLC (*n*-hexane/*i*-propanol = 92/8) $t_R = 24.5$ min.

Acetic acid 8b-methoxy-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta-[c]quinolin-1-yl methyl ester (14b and *ent*-14b):[27b] previously unreported analytical data: $R_f = 0.45$ (EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$)

(36) (a) Acheson, A. M.; Bolton, R. G.; Hunter, I. *J. Chem. Soc. C* **1970**, 1067. (b) Albini, A.; Fasani, E.; Dacrema, L. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2738.

δ 1.99−2.08 (m, 1H, NHCOCHC*H*H), 2.09 (s, 3H, $COCH_3$), 2.21−2.28 (m, 1H, NHCOCHCH*H*), 2.79−2.86 (m, 1H, $COOCH_2CH$), 2.95 (s, 3H, OCH_3), 3.34 (virt. t, ^3J = 9.9 Hz, 1H, NHCOC*H*), 4.36 (dd, ^2J = 11.4 Hz, ^3J = 7.7 Hz, 1H, COOC*H*H), 4.56 (dd, ^2J = 11.4 Hz, ^3J = 6.5 Hz, 1H, COOCH*H*), 6.94 (d, ^3J = 7.9 Hz, 1H, arom. H), 7.14 (virt. dt, ^3J = 7.6 Hz, ^4J = 0.9 Hz, 1H, arom. H), 7.29 (virt. dt, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 1H, arom. H), 7.40 (dd, ^3J = 7.7 Hz, ^4J = 1.1 Hz, 1H, arom. H), 9.97 (s, b, 1H, NH); NOESY-experiment (300 MHz, $CDCl_3$) (see General Information): H (3.34) − H (4.36, 2.95, 2.21−2.28)″; H (2.79−2.86) − H (1.99−2.08)″; H (2.21−2.28) − H (1.99−2.08)‴; H (2.21−2.28) − H (3.34)″; H (1.99−2.08) − H (2.79−2.86)″; H (1.99−2.08) − H (2.21−2.28)‴; ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0 (q, $COCH_3$), 22.1 (t, NHCOCHCH_2), 41.7 (d, NHCO*C*H), 45.2 (d, $COOCH_2CH$), 50.3 (q, OCH_3), 63.4 (t, $COOCH_2$), 76.7 (s, *C*OCH_3), 115.8 (d, CH_{ar}), 123.3 (s, C_{ar}), 124.2 (d, CH_{ar}), 127.9 (d, CH_{ar}), 129.6 (d, CH_{ar}), 137.3 (s, C_{ar}), 171.1, 171.5 (s, 2C, NHCO, COO); MS (EI), *m*/*z* (%) 175 (100), 160 (3), 146 (5), 132 (18), 117 (13), 104 (3), 90 (4), 77 (4), 55 (8), 43 (41).

(−)-**14b**: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 27.0 min. (+)-*ent*-**14b**: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 30.0 min.

Acetic acid 8b-methoxy-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[c]quinolin-1-yl ester (14c, *ent*-14c, 15c, *ent*-15c): R_f = 0.50 (EtOAc); IR (KBr) 2988 (m, CH), 1747 (s, C═O), 1674 (vs, C═O), 1374 (s), 1222 (s); MS (ESI), *m*/*z* 261 [M^+]. Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.10; H, 5.62; N, 5.14.

14c and *ent*-**14c:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (s, 3H, $COCH_3$), 2.27 (ddd, ^2J = 13.3 Hz, ^3J = 9.4 Hz, ^3J = 6.5 Hz, 1H, NHCOCHC*H*H), 2.49 (ddd, ^2J = 13.3 Hz, ^3J = 11.3 Hz, ^3J = 1.9 Hz, 1H, NHCOCHCH*H*), 2.98 (s, 3H, OCH_3), 3.51 (virt. t, ^3J = 10.3 Hz, 1H, NHCOC*H*), 5.15 (m, 1H, COOCH), 6.92 (d, ^3J = 8.0 Hz, 1H, arom. H), 7.15−7.20 (m, 1H, arom. H), 7.31−7.36 (m, 1H, arom. H), 7.62 (dd, ^3J = 7.8 Hz, ^4J = 1.3 Hz, 1H, arom. H), 9.78 (s, b, 1H, NH); NOESY-experiment (500 MHz, $CDCl_3$) (see General Information): H (5.15) − H (7.62, 2.27)‴; H (3.51) −H (2.98)″; H (3.51) − H (2.49)‴; H (2.49) − H (3.51, 2.27)‴; H (2.27) − H (5.15, 2.49)‴; ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9 (q, $COCH_3$), 26.2 (t, NHCOCHCH_2), 41.5 (d, NHCO*C*H), 50.5 (q, OCH_3), 75.9 (d, COO*C*H), 77.1 (s, *C*OMe), 115.7 (d, CH_{ar}), 120.7 (s, C_{ar}), 124.4 (d, CH_{ar}), 129.1 (d, CH_{ar}), 130.2 (d, CH_{ar}), 137.6 (s, C_{ar}), 170.0, 170.9 (s, 2C, NHCO, COO).

14c: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 24.7 min. *ent*-**14c**: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 27.2 min.

15c and *ent*-**15c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.76 (virt. q, $^2J \cong {}^3J \cong$ 10.5 Hz, 1H, NHCOCHC*H*H), 2.00 (s, 3H, $COCH_3$), 2.76 (ddd, ^2J = 11.3 Hz, ^3J = 9.4 Hz, ^3J = 8.4 Hz, 1H, NHCOCHCH*H*), 2.95−3.03 (m, 1H, NHCOC*H*), 3.00 (s, 3H, OCH_3), 5.34 (dd, ^3J = 9.3 Hz, ^3J = 8.5 Hz, 1H, COOCH), 6.97 (d, ^3J = 7.8 Hz, 1H, arom. H), 7.12−7.17 (m, 1H, arom. H), 7.30−7.38 (m, 2H. arom. H), 9.78 (s, b, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8 (q, $COCH_3$), 26.7 (t, NHCOCHCH_2), 37.7 (d, NHCO*C*H), 51.3 (q, OCH_3), 72.9 (d, COO*C*H), 81.9 (s, *C*OCH_3), 116.1 (d, CH_{ar}), 116.4 (s, C_{ar}), 123.4 (d, CH_{ar}), 130.2 (d, CH_{ar}), 130.7 (d, CH_{ar}), 138.0 (s, C_{ar}), 169.8, 170.8 (s, 2C, NHCO, COO).

15c: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 36.8 min. *ent*-**15c**: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 40.2 min.

8b-Methoxy-1-phenyl-2,2a,4,8b-tetrahydro-1H-cyclobuta[c]quinolin-3-one (15d and *ent*-15d): R_f = 0.46 (EtOAc); mp 217−219 °C; IR (KBr) 2983 (m, CH), 1673 (s, C═O), 1592 (m), 1488 (m), 1395 (m), 1116 (m); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.09 (virt. q, $^2J \cong {}^3J \cong$ 10.9 Hz, 1H, NHCOCHC*H*H), 2.58 (virt. q, $^2J \cong {}^3J \cong$ 9.8 Hz, 1H, NHCOCHCH*H*), 3.00 (s, 3H, CH_3), 3.31 (virt. t, ^3J = 9.6 Hz, 1H, NHCOC*H*), 4.06 (dd, ^3J = 11.6 Hz, ^3J = 9.2 Hz, 1H, NHCOCHCH_2C*H*), 6.36 (d, ^3J = 7.6 Hz, 1H, arom. H), 6.67 (virt. t, ^3J = 7.4 Hz, 1H, arom. H), 6.88−6.96 (m, 3H, arom. H), 7.13−7.27 (m, 4H, arom. H), 9.65 (s, b, 1H, NH); NOESY-experiment (500 MHz, $CDCl_3$) (see General Information): H (4.06) − H (3.31, 2.58)″; H (3.31) − H (4.06, 3.00, 2.58)″; H (2.58) − H (4.06, 3.31)″; H (2.58) − H (2.09)‴; H (2.79) − H (2.58)‴; ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.9 (t, NHCOCHCH_2), 42.2 (d, NHCOCHCH_2CH), 51.1 (q, CH_3), 52.6 (d, NHCO*C*H), 82.2 (s, *C*OCH_3), 115.6 (d, CH_{ar}), 117.8 (s, C_{ar}), 122.7 (d, CH_{ar}), 127.1 (d, CH_{ar}), 127.9 (d, 2C, CH_{ar}), 128.6 (d, 2C, CH_{ar}), 129.5 (d, CH_{ar}), 130.8 (d, CH_{ar}), 137.5 (s, C_{ar}), 138.2 (s, C_{ar}), 171.6 (s, CO); MS (EI), *m*/*z* (%) 175 (100), 132 (9), 117 (7), 104 (5), 90 (1); Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found C, 77.08; H, 6.39; N, 5.31.

15d: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 25.0 min. *ent*-**15d**: HPLC (*n*-hexane/*i*-propanol = 93/7) t_R = 39.5 min.

8b-Methoxy-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[c]quinolin-1-carboxylic acid methyl ester (14e and *ent*-14e):[30a] previously unreported analytical data: R_f = 0.47 (EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.00 (virt. dt, ^2J = 11.9 Hz, ^3J = 8.7 Hz, 1H, NHCOCHC*H*H), 2.79 (ddd, ^2J = 11.9 Hz, ^3J = 11.1 Hz, ^3J = 3.4 Hz, 1H, NHCOCHCH*H*), 2.95 (s, 3H, $COCH_3$), 3.37−3.41 (m, 1H, NHCOCH-CH_2C*H*), 3.61 (virt. t, ^3J = 10.0 Hz, 1H, NHCOC*H*), 6.90 (dd, ^3J = 8.1 Hz, ^4J = 0.9 Hz, 1H, arom. H), 7.16 (virt. dt, ^3J = 7.6 Hz, ^4J = 1.1 Hz, 1H, arom. H), 7.32 (virt. dt, ^3J = 7.6 Hz, ^4J = 1.5 Hz, 1H, arom. H), 7.51 (dd, ^3J = 7.7 Hz, ^4J = 1.3 Hz, 1H, arom. H), 9.48 (s, b, 1H, NH); NOESY-experiment (500 MHz, $CDCl_3$) (see General Information): H (3.61) − H (2.95, 2.79)″; H (3.61) − H (2.00)′; H (3.37−3.41) − H (2.00)″; H (2.79) − H (3.61)″; H (2.79) − H (2.00)‴; H (2.00) − H (3.61)′; H (2.00) − H (3.37−3.41)″; H (2.00) − H (2.79)‴;^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0 (t, NHCOCHCH_2), 42.0 (d, NHCO*C*H), 50.6 (d, NHCOCHCH_2CH), 51.0 (q, $COCH_3$), 52.1 (q, $COOCH_3$), 77.0 (s, *C*OCH_3), 115.8 (d, CH_{ar}), 122.2 (s, C_{ar}), 124.4 (d, CH_{ar}), 128.2 (d, CH_{ar}), 130.1 (d, CH_{ar}), 137.3 (s, C_{ar}), 170.8, 171.4 (s, 2C, *C*$OOCH_3$, NH*C*O); MS (EI), *m*/*z* (%): 261 (1) [M^+], 201 (2), 175 (100), 146 (2), 132 (13), 117 (10), 90 (2), 77 (2), 55 (10).

14e: HPLC (*n*-hexane/*i*-propanol = 92/8) t_R = 21.6 min. *ent*-**14e**: HPLC (*n*-hexane/*i*-propanol = 92/8) t_R = 21.6 min.

1,1-Diethyl-8b-methoxy-2,2a,4,8b-tetrahydro-1H-cyclobuta[c]-quinolin-3-one (14f and *ent*-14f): R_f = 0.50 (EtOAc); mp 122−124 °C; IR (KBr) 2964 (m, CH), 1674 (s, C═O), 1377 (s), 1101 (m); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 0.66 (virt. t, ^3J = 7.4 Hz, 3H, CH_2CH_3), 0.88 (dq, ^2J = 14.0 Hz, ^3J = 7.1 Hz, 1H, C*H*HCH$_3$), 0.98 (virt. t, ^3J = 7.4 Hz, 3H, CH_2CH_3), 1.40 (dq, ^2J = 14.0 Hz, ^3J = 7.1 Hz, 1H, CH*H*CH$_3$), 1.51 (dq, ^2J = 14.1 Hz, ^3J = 7.2 Hz, 1H, C*H*HCH$_3$), 1.59 (dd, ^2J = 11.5 Hz, ^3J = 8.8 Hz, 1H, NHCOCHC*H*H), 2.11 (dq, ^2J = 14.1 Hz, ^3J = 7.2 Hz, 1H, CH*H*CH$_3$), 2.16 (virt. t, $^2J \cong {}^3J \cong$ 11.3 Hz, 1H, NHCOCHCH*H*), 2.92 (s, 3H, OCH_3), 3.28 (dd, ^3J = 11.1 Hz, ^3J = 8.8 Hz, 1H, NHCOC*H*), 6.95 (d, ^3J = 7.7 Hz, 1H, arom. H), 7.07 (virt. dt, ^3J = 7.4 Hz, ^4J = 1.1 Hz, 1H, arom. H), 7.21−7.27 (m, 2H, arom. H), 10.08 (s, b, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.8 (q, CH_2CH_3), 9.5 (q, CH_2CH_3), 25.3 (t, *C*H_2CH$_3$), 27.3 (t, *C*H_2CH$_3$), 32.5 (t, NHCOCHCH_2), 39.0 (d, NHCO*C*H), 50.5 (s, CH_3CH_2C), 50.6 (q, OCH_3), 82.6 (s, *C*OCH_3), 116.0 (d, CH_{ar}), 120.4 (s, C_{ar}), 123.0 (d, CH_{ar}), 129.0 (d, CH_{ar}), 129.4 (d, CH_{ar}), 138.1 (s, C_{ar}), 172.8 (s, CO); MS (EI), *m*/*z* (%) 259 (<1) [M^+], 188 (4), 175 (100), 132 (4), 117 (3). HRMS (EI) calcd for $C_{16}H_{21}NO_2$: 259.1572, found 259.1571; for C_{15}-$^{13}CH_{21}NO_2$: calcd. 260.1606, found 260.1611.

14f: HPLC (*n*-hexane/*i*-propanol = 95/5) t_R = 14.7 min. *ent*-**14f**: HPLC (*n*-hexane/*i*-propanol = 95/5) t_R = 22.5 min.

Reduction of Methyl Ester 14e to the Corresponding Alcohol: (8b-Methoxy-1,2,2a,3,4,8b-hexahydrocyclobuta[c]quinolin-1-yl)-methanol. The mixture of methyl esters **14e** and *ent*-**14e** obtained by irradiation (37 mg, 0.14 mmol) was dissolved in a mixture of THF (10 mL) and ethanol (10 mL), and $LiBH_4$ (80 mg, 3.67 mmol) was added. After the solution was stirred at room temperature for 18 h, water (10 mL) was added, and the solvents were evaporated. The residue was partitioned between water (10 mL) and CH_2Cl_2 (10 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and evaporated. The crude material was purified by flash chromatography (TBME/pentane = 3/2) to give

a white solid (15 mg, 50%): $R_f = 0.48$ (pentane/TBME = 1/3); mp 78−79 °C; IR (KBr) 3531 (m, NH), 3339 (m, NH), 2932 (m CH), 1610 (m), 1494 (s), 1302 (m), 1105 (s), 1038 (s); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49 (ddd, ^2J = 11.7 Hz, ^3J = 9.9 Hz, ^3J = 3.1 Hz, 1H, $NHCH_2CHCHH$), 1.81 (virt. dt, ^2J = 11.7 Hz, ^3J = 9.0 Hz, 1H, $NHCH_2CHCHH$), 2.36−2.44 (m, 1H, $NHCH_2CH$), 2.94−3.00 (m, 1H, $HOCH_2CH$), 3.09 (s, 3H, OCH_3), 3.10−3.13 (m, 2H, $HOCHH$), 3.75 (b, d, ^2J = 9.7 Hz, 1H, $NHCHH$), 4.00 (dd, ^2J = 9.7 Hz, ^3J = 11.2 Hz, 1H, $NHCHH$), 6.61 (d, ^3J = 8.1 Hz, 1H, arom. H), 6.80 (virt. t, ^3J = 7.4 Hz, 1H, arom. H), 7.07 (virt. dt, ^3J = 7.6 Hz, ^4J = 1.5 Hz, 1H, arom. H), 7.33 (dd, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1H, arom. H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 15.7 (t, $NHCH_2CHCH_2$), 39.1 (d, $HOCH_2CH$), 42.4 (t, $HOCH_2$), 47.5 (d, $NHCH_2CH$), 51.1 (q, OCH_3), 64.6 (t, $NHCH_2$), 76.1 (s, $COCH_3$), 114.9 (d, CH_{ar}), 119.0 (d, CH_{ar}), 124.1 (s, C_{ar}), 128.0 (d, CH_{ar}), 128.1 d, CH_{ar}), 145.3 (s, C_{ar}); MS (EI), *m*/*z* (%) 219 (2) [M^+], 185 (4), 160 (100), 130 (9), 77 (4); HRMS (EI) calcd for $C_{13}H_{17}NO_2$: 219.1259, found 219.1258; for $C_{12}\,^{13}CH_{17}NO_2$: calcd 220.1293, found 220.1288.

Reduced **14e**: HPLC (*n*-hexane/*i*-propanol = 92/8) t_R = 26.3 min. Reduced *ent*-**14e**: HPLC (*n*-hexane/*i*-propanol = 92/8) t_R = 24.3 min.

Silyl Ether *rac*-16 by Silylation of Alcohol *rac*-14a. To a solution of alcohol *rac*-**14a** (175 mg, 0.70 mmol) and imidazole (52 mg, 0.76 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added dropwise a solution of TBDMSCl in toluene (266 μL, 2.9 M in toluene, 0.77 mmol). After the mixture was stirred for 2 h at 0 °C, another portion of imidazole (52 mg, 0.76 mmol) and TBDMSCl (266 μL, 2.9 M in toluene, 0.77 mmol) were added. After 1 h the cloudy solution was filtered, and the solvent was removed in vacuo. Without further workup the crude product was purified by flash chromatography (TBME/pentane = 2/3) to give a white solid (194 mg, 77%): $R_f = 0.19$ (pentane/TBME = 1/1); mp 118−119 °C; IR (KBr) 2931 (s, CH), 1680 (vs, C=O), 1593 (m), 1378 (s), 1254 (m), 1100 (m); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 [s, 6H, $Si(CH_3)_2$], 0.91 (s, 9H, $C(CH_3)_3$), 1.50−1.68 (m, 3H, $SiOCH_2CHH$, $NHCOCHCH$), 1.89−2.12 (m, 3H, $SiOCH_2CH_2CHH$, $NHCOCHCHH$), 2.42−2.53 (m, 1H, $NHCOCHCH_2CH$), 2.94 (s, 3H, OCH_3), 3.34 (virt. t, ^3J = 9.6 Hz, 1H, $NHCOCH$), 3.60−3.70 (m, 2H, $SiOCHH$), 6.94 (d, ^3J = 7.8 Hz, 1H, arom. H), 7.11 (virt. dt, ^3J = 7.4 Hz, ^4J = 1.0 Hz, 1H, arom H.), 7.24 (virt. dt, ^3J = 7.7 Hz, ^4J = 1.2 Hz, 1H, arom. H), 7.36 (dd, ^3J = 7.6 Hz, ^4J = 1.0 Hz, 1H, arom. H), 10.23 (s, b, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.3 [q, 2C, $Si(CH_3)_2$], 18.4 [s, $C(CH_3)_3$], 24.7 (t, $SiOCH_2CH_2CH_2$), 26.0 [q, 3C, $C(CH_3)_3$], 26.1 (t, $NHCOCHCH_2$), 30.7 (t, $SiOCH_2CH_2$), 41.5 (d, $NHCOCH$), 47.1 (d, $NHCOCHCH_2CH$), 50.3 (q, OCH_3), 63.3 (t, $SiOCH_2$), 77.0 (s, $COCH_3$), 115.8 (d, CH_{ar}), 124.0 (d, CH_{ar}), 124.6 (s, C_{ar}), 127.8 (d, CH_{ar}), 129.2 (d, CH_{ar}), 137.4 (s, C_{ar}), 172.4 (s, CO); MS (FD), *m*/*z* (%) 375 (18) [M^+], 374 (82), 317 (45), 175 (100). Anal. Calcd for $C_{21}H_{33}NO_3Si$: C, 67.16; H, 8.86; N, 3.73. Found: C, 66.92; H, 8.68; N, 3.94.

Single-crystal X-ray crystallography of compound 16: crystal data of compound **16** ($C_{21}H_{33}NO_3Si$, M_r = 357.57): crystal size 0.54 × 0.18 × 0.18 mm^3, triclinic, space group $P\bar{1}$, a = 766.5(1) pm, b = 1164.4(1) pm, c = 1260.6(1) pm, α = 98.67(1)°, β = 105.09(1)°, γ = 97.31(1)°, U = 1057.8(2) Å^3, D_c = 1.179 g cm^{-3} for Z = 2, F(000) = 408, μ = 1.128 mm^{-1}, Enraf Nonius CAD4 diffractometer, λ = 1.54178 Å, T = 203 K, ω-scan, 4313 reflections (h, $+k$, $\pm l$), Θ_{max} = 70.1°, 3995 independent and 2877 observed reflections [$F \geq 4\sigma(F)$], 245 refined parameters, R = 0.0628 (observed data), wR^2 = 0.1756 (independent data), residual electron density 0.452 eÅ^{-3}, direct methods, carbon-bonded hydrogen atoms calculated, N−H refined (SHELXS-97, SHELXL-97, SHELXTL). Crystallographic data for the structures reported in this work have been deposited as a CIF file (see Supporting Information).

Isothermal Titration Calorimetry (ITC).[37] The measurements were performed with a MCT-ITC instrument (MicroCal) at 303 K; 100 injections (injection volume: 2 μL, injection duration: 8.72 s, time between injections: 100 s) of a degassed 220 mM solution of host **5** (44 μmol) were performed into the cell containing 1.4 mL of a degassed solution of 2-quinolone (**17**) in toluene (Merck p.a.) (1.4 mL, 10 mM, 14 μmol). By integration of each heat pulse at each titration step the titration curve was derived, giving ΔH_a directly as a primary parameter of measurement. The heat of dilution was corrected for by injecting the host solution into neat toluene and subtracting these data from those of the host−guest titration. ΔG_a and the host−guest stoichiometry were estimated from the titration curve by curve-fitting with ITC Data Analysis (MicroCal).

NMR Titration Experiments. All titrations were conducted at 293 K in d^8-toluene (Aldrich) on a Bruker AMX-500 instument. Chemical shifts were determined relative to the solvent. The HOSTEST program (version 5.60) was used for determining the self-association constant of host *ent*-**5** to 0 ± 0.2 M^{-1}. The association constant of host **5** with quinolone **17** was calculated by optimized curve-fitting with HOSTEST including dimerization of both compounds. The best curve-fit was obtained with a self-association constant for **17** of K_{dim} = 41 M^{-1}, giving an association constant of **5**/**17** of K_a = 580 ± 11 M^{-1}. Limits of errors given here refer to the standard deviation as calculated by the program.

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Supporting Information Available: Detailed analytical data of all irradiation products, results of the ^{1}H NMR titration (curve fits by HOSTEST) and of the microcalorimetry measurements, and calculation of ee values from K_a (PDF). Two X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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